

JCO9 Rec'd PCT/PTO 01 NOV 2001

FORM PTO-1390 (REV. 9-2001)		U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE		ATTORNEY'S DOCKET NUMBER
				BER-3.2.050/4167
		TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371		U.S. APPLICATION NO. (If known, see 37 CFR 1.5
INTERNATIONAL APPLICATION NO. PCT/GB00/01728		INTERNATIONAL FILING DATE 05 MAY 2000		10/01816D
				PRIORITY DATE CLAIMED 06 MAY 1999
TITLE OF INVENTION A METHOD AND APPARATUS FOR MANUFACTURING DISSOLVABLE TABLETS				
APPLICANT(S) FOR DO/EO/US Ronald Alan COFFEE, Alastair Bruce PIRRIE & David Neville DAVIES				
Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:				
<p>1. <input checked="" type="checkbox"/> This is a FIRST submission of items concerning a filing under 35 U.S.C. 371.</p> <p>2. <input type="checkbox"/> This is a SECOND or SUBSEQUENT submission of items concerning a filing under 35 U.S.C. 371.</p> <p>3. <input checked="" type="checkbox"/> This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.</p> <p>4. <input type="checkbox"/> The US has been elected by the expiration of 19 months from the priority date (Article 31).</p> <p>5. <input checked="" type="checkbox"/> A copy of the International Application as filed (35 U.S.C. 371(c)(2))</p> <ul style="list-style-type: none"> a. <input type="checkbox"/> is attached hereto (required only if not communicated by the International Bureau). b. <input checked="" type="checkbox"/> has been communicated by the International Bureau. c. <input type="checkbox"/> is not required, as the application was filed in the United States Receiving Office (RO/US). <p>6. <input checked="" type="checkbox"/> An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).</p> <ul style="list-style-type: none"> a. <input type="checkbox"/> is attached hereto. b. <input type="checkbox"/> has been previously submitted under 35 U.S.C. 154(d)(4). <p>7. <input type="checkbox"/> Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))</p> <ul style="list-style-type: none"> a. <input type="checkbox"/> are attached hereto (required only if not communicated by the International Bureau). b. <input type="checkbox"/> have been communicated by the International Bureau. c. <input type="checkbox"/> have not been made; however, the time limit for making such amendments has NOT expired. d. <input type="checkbox"/> have not been made and will not be made. <p>8. <input type="checkbox"/> An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).</p> <p>9. <input checked="" type="checkbox"/> An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).</p> <p>10. <input type="checkbox"/> An English language translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).</p>				
Items 11 to 20 below concern document(s) or information included:				
<p>11. <input checked="" type="checkbox"/> An Information Disclosure Statement under 37 CFR 1.97 and 1.98.</p> <p>12. <input checked="" type="checkbox"/> An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.</p> <p>13. <input checked="" type="checkbox"/> A FIRST preliminary amendment.</p> <p>14. <input type="checkbox"/> A SECOND or SUBSEQUENT preliminary amendment.</p> <p>15. <input type="checkbox"/> A substitute specification.</p> <p>16. <input type="checkbox"/> A change of power of attorney and/or address letter.</p> <p>17. <input type="checkbox"/> A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 - 1.825.</p> <p>18. <input type="checkbox"/> A second copy of the published international application under 35 U.S.C. 154(d)(4).</p> <p>19. <input type="checkbox"/> A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).</p> <p>20. <input checked="" type="checkbox"/> Other items or information: Certificate of Express Mail</p>				

U.S. APPLICATION NO. (if known, see 37 CFR 1.491)		INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER																									
10/018160		PCT/GB00/01728	BER-3.2.050/4167																									
<input checked="" type="checkbox"/> The following fees are submitted: BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)): Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO \$1040.00 International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO \$890.00 International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO \$740.00 International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) \$710.00 International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) \$100.00		CALCULATIONS PTO USE ONLY																										
ENTER APPROPRIATE BASIC FEE AMOUNT =		\$ 890																										
Surcharge of \$130.00 for furnishing the oath or declaration later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(e)). <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th>CLAIMS</th> <th>NUMBER FILED</th> <th>NUMBER EXTRA</th> <th>RATE</th> <th>\$</th> </tr> </thead> <tbody> <tr> <td>Total claims</td> <td>43 - 20 =</td> <td>23</td> <td>x \$18.00</td> <td>\$ 414</td> </tr> <tr> <td>Independent claims</td> <td>4 - 3 =</td> <td>1</td> <td>x \$84.00</td> <td>\$ 84</td> </tr> <tr> <td colspan="2">MULTIPLE DEPENDENT CLAIM(S) (if applicable)</td> <td></td> <td>+ \$280.00</td> <td>\$</td> </tr> <tr> <td colspan="2"></td> <td></td> <td style="text-align: right;">TOTAL OF ABOVE CALCULATIONS =</td> <td>\$ 1388</td> </tr> </tbody> </table>		CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	\$	Total claims	43 - 20 =	23	x \$18.00	\$ 414	Independent claims	4 - 3 =	1	x \$84.00	\$ 84	MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ \$280.00	\$				TOTAL OF ABOVE CALCULATIONS =	\$ 1388		
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<input type="checkbox"/> Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2. SUBTOTAL = \$ 1388																												
Processing fee of \$130.00 for furnishing the English translation later than <input type="checkbox"/> 20 <input type="checkbox"/> 30 months from the earliest claimed priority date (37 CFR 1.492(f)). TOTAL NATIONAL FEE = \$ 1388																												
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). \$40.00 per property + \$ 40																												
TOTAL FEES ENCLOSED = \$ 1428																												
		Amount to be refunded:	\$																									
		charged:	\$																									
a. <input checked="" type="checkbox"/> A check in the amount of \$ 1428.00 to cover the above fees is enclosed. b. <input type="checkbox"/> Please charge my Deposit Account No. _____ in the amount of \$ _____ to cover the above fees. A duplicate copy of this sheet is enclosed. c. <input checked="" type="checkbox"/> The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. <u>03-2317</u> . A duplicate copy of this sheet is enclosed. d. <input type="checkbox"/> Fees are to be charged to a credit card. WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.																												
NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.																												
SEND ALL CORRESPONDENCE TO: COBRIN & GITTES 750 LEXINGTON AVE -- 21 FL NEW YORK, NY 10022																												
 SIGNATURE ROBERT J. HESS NAME 32,139 REGISTRATION NUMBER																												
Tel: (212) 486-4000 Fax: (212) 486-4007																												

10/01816D

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

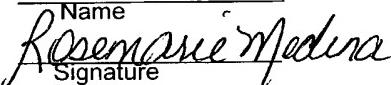
Inventors : Ronald Alan COFFEE et al X
Assignee : Electrosols Ltd.
US National Phase of PCT/GB00/01728 Published November 16, 2000
USSN : To be assigned
Filed : Concurrently herewith (November 1, 2001)
Title : A METHOD AND APPARATUS FOR MANUFACTURING DISSOLVABLE TABLETS
Art Unit : To be assigned
Examiner : To be assigned X

BOX PCT-RO (DO/EO/US)
Assistant Commissioner for Patents
US Patent and Trademark Office
Washington, DC 20231

Sir:

PRELIMINARY AMENDMENT

Prior to examining the above referenced Application on the merits, please amend the Application as follows:

MAILING CERTIFICATE	
I hereby certify that this correspondence is being deposited with the United States Postal Service as EXPRESS MAIL LABEL EL781390550USI in an envelope addressed to: BOX PCT-RO (DO/EO/US), FEE - Assistant Commissioner for Patents, Washington, DC 20231 on the date indicated below:	
_____ Rosemarie Medina Name  _____ Signature _____ November 1, 2001 Date	

ABSTRACT OF THE DISCLOSURE:

Cancel the current abstract of the disclosure and replace it at the back of the Application with the accompanying new Abstract of the Disclosure.

IN THE CLAIMS:

Pursuant to 37 CFR § 1.121(c)(1)(i), herein below are a set of clean claims containing all revisions made herein.

Cancel Claims 1 - 3, 10 and 17 without prejudice.

Amend the Claims as follows:

4. (Once amended) A method according to claim 34, wherein the supplying includes providing the liquid as a composition selected from a group consisting of a gelatin, a starch, cellulose, a cellulose derivative, a water-soluble polymer, polyvinyl pyrrolidone, polyvinyl alcohol, poly-sucrose, and a sugar.
5. (Once amended) A method according to claim 34, wherein the supplying includes providing as the liquid a solution consisting essentially of 5 grams of fish gelatin in a solvent consisting of from 7 to 9 milliliters of water and 10 to 11 milliliters of ethanol.
6. (Once amended) A method according to claim 34, which comprises supplying as the liquid a solution consisting essentially of 5 grams of fish gelatin in a solvent

consisting of 8 milliliters of water, 10 milliliters of ethanol and 1 milliliter of peppermint flavoring.

7. (Once amended) A method according to claim 34, which comprises providing an air flow to encourage the deposition of the at least one fiber or fibrils on the surface.
8. (Once amended) A method according to claim 34, which further comprises regulating temperature of a region where the liquid issues from the outlet to facilitate the formation of the at least one fiber or fibrils.
9. (Once amended) A method according to claim 34, which comprises establishing the electric field by applying a high voltage to the surface.
11. (Once amended) A method according to claim 34, which further comprises using as the surface a rotatable endless surface].
12. (Once amended) A method according to claim 34, wherein the providing of the at least one active ingredient is effected by spraying the active ingredient onto at least one of: the at least one fiber or fibrils; the mat or web; and the individual tablets.
13. (Once amended) A method according to claim 34, wherein the providing of the active ingredient is incorporated into the at least one fiber or fibrils.

- 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
14. (Once amended) A method according to claim 34, which further comprises forming the at least one fiber or fibrils with a core containing the at least one active ingredient.
15. (Once amended) A method of manufacturing a pharmaceutical product which further comprises using a method in accordance with claim 34 and providing as the at least one active ingredient an ingredient which is pharmacologically or biologically active.
16. (Once amended) A method of manufacturing a confectionary product which comprises using a method in accordance with claim 34 to form the plurality of individual tablets and incorporating as the at least one active ingredient at least one of the following: sugar; chocolate; a flavoring; and a colorant.
18. (Once amended) Apparatus according to claim 48, wherein the cutting means comprises at least one cutter.
19. (Once amended) Apparatus for manufacturing consumable or dissolvable tablets, comprising:
means for supplying a liquid containing a biodissolvable carrier through a liquid supply tube to an outlet of the tube;

means for establishing an electric field between the outlet and a support surface spaced from the outlet to cause liquid issuing from the outlet to form at least one fiber or fibrils of the biodissolvable carrier;

means for causing the fiber or fibrils to deposit onto the support surface to form a fiber web or mat;

means for forming from the fiber web or mat a plurality of individual tablets; and

means for incorporating at least one active ingredient into the web or mat, the individual tablets being configured to melt, liquefy, disintegrate or dissolve in a wet environment.

20. (Once amended) Apparatus according to claim 19, wherein the liquid is a supply selected from a group consisting of a gelatin, starch, cellulose, a cellulose derivative, a water soluble polymer, polyvinyl pyrrolidone, polyvinyl alcohol, polysucrose, a sugar.
21. (Once amended) Apparatus according to claim 19, wherein the liquid is a supply selected from a group consisting of a solution consisting essentially of 5 grams of gelatin in 7 to 9 milliliters of water and 10 to 11 milliliters of ethanol.
22. (Once amended) Apparatus according to claim 19, wherein the liquid is a supply of a solution consisting essentially of 5 grams of gelatin in 8 milliliters of water, 10 milliliters of ethanol and 1 milliliter of peppermint flavoring.

3. C1 C2 4. C3 4. C5 C6 5. C1 C2 C3 C4
23. (Once amended) Apparatus according to claim 19, further comprising air flow causing means for facilitating the deposition of the at least one fiber or fibrils onto the support.
24. (Once amended) Apparatus according to claim 19, wherein the electric field establishing means comprises means for applying a positive potential to the support.
25. (Once amended) Apparatus according to claim 19, further comprising a rotatable endless surface as the support.
26. (Once amended) Apparatus according to claim 19, further comprising an environmental control means for regulating the temperature of the region where liquid issues from the outlet.
27. (Once amended) Apparatus according to claim 19, further comprising spraying means for spraying the at least one active ingredient onto at least one of: the fiber or fibrils; the mat or web; and individual tablets.
28. (Once amended) Apparatus according to claim 19, further comprising means for supplying the active ingredient so that the at least one fiber or fibrils have a core containing the active ingredient.

- 23 23 23 23 23 23 23 23 23 23 23 23 23 23 23 23
29. (Once amended) A consumable or dissolvable tablet, pad or mat manufactured using a method in accordance with claim 34.
30. (Once amended) A consumable or dissolvable tablet produced by subjecting liquid comprising the carrier material to a high electric field and comprising a web of fibers of a carrier material carrying at least one active ingredient, the carrier material being configured and arranged to melt, liquefy, dissolve or disintegrate in a wet environment.
31. (Once amended) A consumable or dissolvable tablet of claim 30, wherein the web of fibers or fibrils are of gelatin, the liquid comprising gelatin.
32. (Once amended) A tablet according to claim 30, wherein the active ingredient comprises a pharmacologically or biologically active ingredient.

Insert the following new Claims 34-48:

34. (Newly submitted) A method of manufacturing tablets, comprising supplying a liquid containing a carrier through a supply tube to an outlet of the supply tube, establishing an electric field between the outlet and a support surface that is spaced from the outlet to cause liquid issuing from the outlet to form at least one fiber or fibrils of the carrier, causing the at least one fiber or fibrils to deposit onto the support surface to form a fiber web or mat, forming a plurality of individual tablets

from the fiber or mat, and providing the individual tablets with at least one active ingredient, the individual tablets melting, liquefying, disintegrating or dissolving in a wet environment.

35. (Newly submitted) A method as in claim 34, wherein the forming arising from separating the fiber web or mat into the plurality of individual tablets.
36. (Newly submitted) A method as in claim 35, wherein the separating is effected by cutting the fiber web or mat.
37. (Newly submitted) A method as in claim 34, wherein the carrier is biodissolvable.
38. (Newly submitted) A method as in claim 34, wherein the carrier is hydrophilic and biologically compatible.
39. (Newly submitted) A method as in claim 34, wherein the fiber web or mat is configured to melt or liquefy on contact with a wet surface.
40. (Newly submitted) A method as in claim 34, wherein the providing of the individual tablets with at least one active ingredient includes incorporating the at least one active ingredient in and/or on the individual tablets.

- 2 1 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
41. (Newly submitted) A method as in claim 34, wherein the liquid consists essentially of a hydrophilic solution of gelatin, the deposit causing formation on the support surface of the fiber web or mat, the fiber web or mat consisting of at least one gelatin fiber as the afore-mentioned fiber or gelatin fibrils as the afore-mentioned fibrils, the forming of the individual tablets arising from separating the fiber web or mat, the providing of the at least one active ingredient including incorporating the at least one active ingredient and a sweetener into and/or on the individual tablets.
42. (Newly submitted) A method as in claim 41, wherein the sweetener is saccharine.
43. (Newly submitted) An apparatus as in claim 19, further comprising means for separating the web or mat into the plurality of individual tablets, the means for incorporating including means for incorporating the at least one active ingredient in the tablets.
44. (Newly submitted) A consumable or dissolvable tablet as in claim 30, wherein the carrier material is biodissolvable.
45. (Newly submitted) A method as in claim 34, wherein the liquid consists essentially of a hydrophilic solution of gelatin, the deposit causing formation on the support surface of the fiber web or mat, the fiber web or mat consisting of at least one gelatin fiber as the afore-mentioned fiber or gelatin fibrils as the afore-mentioned fibrils, the forming of the individual tablets arising from separating the fiber web or

mat, the providing of the at least one active ingredient including incorporating the at least one active ingredient and a sweetener into and/or on the individual tablets..

46. (Newly submitted) A consumable or dissolvable tablet, pad or mat manufactured using an apparatus in accordance with claim 19.
47. (Newly submitted) An apparatus as in claim 19, wherein the means for forming includes means for separating the individual tablets from the fiber web or mat.
48. (Newly submitted) An apparatus as in claim 47, wherein the means for separating includes means for cutting the fiber web or mat.

R E M A R K S

For convenience of the Examiner set forth below is the current status of the claims in the Application:

Claim	Status	Dependency
1-3	Canceled	--
4-9	Once amended	35
10	Canceled	--
11-16	Once amended	35
17	Canceled	---
18	Once amended	48
19	Once amended	Independent

Claim	Status	Dependency
20-28	Once amended	19
29	Once amended	34
30	Once amended	Independent
31-32	Once amended	30
33	Unchanged	Independent
34	Newly submitted	Independent
35	Newly submitted	34
36	Newly submitted	35
37-41	Newly submitted	34
42	Newly submitted	41
43	Newly submitted	19
44	Newly submitted	30
45	Newly submitted	34
46-47	Newly submitted	19
48	Newly submitted	47

Claims 4-9, 11-32 have been amended to eliminate multiple dependencies and to correct minor linguistic spellings. Claim 29 was amended to become two claims: Claim 29 and newly submitted Claim 49. Claims 1-3 and 10 were canceled replaced by new Claims 34-43. Claim 17 was canceled. New claims 44-48 were also added to recite the same subject matter taken out of other claims.

An Abstract of the Disclosure has been added and is annexed to this Amendment.

In addition to a filing fee of \$890.00 (37 CFR 1.482), enclosed is a check in the total amount of \$1,428 to cover 23 additional total claims (\$414) and 1 additional independent claim (\$84) plus an Assignment recordal fee (\$40). The Commissioner is authorized to credit any overpayment or to debit any deficiency to Deposit Account 03-2317.

Respectfully submitted,

By: 
Robert J. Hess
Attorney of Record
USPTO Reg. 32,139

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Enclosures

~~37 CFR § 1.121(c)(1)(ii)~~

MARKED-UP VERSION OF AMENDED CLAIMS
PURSUANT TO 37 CFR § 1.121(c)(1)(ii)

4. (Once amended) A method according to claim 34, [any one of the proceeding claims, which comprises supplying to provide the] wherein the supplying includes providing the liquid as a composition [comprising at least one] selected from a group consisting of a gelatin, a starch, cellulose, a cellulose derivative, a water-soluble polymer, [such as] polyvinyl pyrrolidone, polyvinyl alcohol, poly-sucrose, and a sugar.
5. (Once amended) A method according to claim 34, [any one of claims 1 to 3, which comprises] wherein the supplying includes providing as the liquid a solution consisting essentially of 5 grams of fish gelatin in a solvent consisting of from 7 to 9 milliliters [millilitres] of water and 10 to 11 [milliliters] milliliters of ethanol.
6. (Once amended) A method according to claim 34, [any one of claims 1 to 3], which comprises supplying as the liquid a solution consisting essentially of 5 grams of fish gelatin in a solvent consisting of 8 [millilitres] milliliters of water, 10 [millilitres] milliliters of ethanol and 1 [millilitre] milliliter of peppermint [flavouring] flavoring.
7. (Once amended) A method according to claim 34, [any one of the preceding claims,] which [comprising] comprises providing an air flow to encourage the deposition of the at least one [fibre] fiber or fibrils on the surface.

8. (Once amended) A method according to claim 34, [any one of the preceding claims,] which further comprises regulating [the] temperature [, for example by applying heat,] of [the] a region where the liquid issues from the outlet to facilitate the formation of the at least one [fibre] fiber or fibrils.
9. (Once amended) A method according to claim 34, [any one of the preceding claims,] which comprises establishing the electric field by applying a high voltage to the surface.
11. (Once amended) A method according to claim 34, [any one of the preceding claims,] which further comprises using as the surface a rotatable endless surface [such as a belt].
12. (Once amended) A method according to claim 34, [any one of the preceding claims,] [which comprises incorporating] wherein the providing of the at least one active ingredient is effected by spraying the active ingredient onto at least one of: the at least one [fibre] fiber or fibrils; the mat or web; and the individual tablets.
13. (Once amended) A method according to claim 34, [any one of the preceding claims,] [which comprises incorporating] wherein the providing of the active ingredient is incorporated into the at least one [fibre] fiber or fibrils.

14. (Once amended) A method according to claim 34, [any one of the preceding claims,] which further comprises forming the at least one [fibre] fiber [of] or fibrils with a core containing [an] the at least one active ingredient.
15. (Once amended) A method of manufacturing a pharmaceutical product which further comprises using a method in accordance with claim 34 [any one of the preceding claims] and providing as the at least one active ingredient an ingredient which is pharmacologically or biologically active.
16. (Once amended) A method of manufacturing a confectionary product which comprises using a method in accordance with claim 34 [any one of claims 1 to 14] to form [a] the plurality of individual tablets and incorporating as the at least one active ingredient at least one of the following: sugar; chocolate; a [flavouring] flavoring; and a colorant.
18. (Once amended) Apparatus according to [claim 17] claim 48, wherein the cutting means comprises at least one cutter.
19. (Once amended) Apparatus for manufacturing consumable or dissolvable tablets, comprising:
means for supplying a liquid containing a biodissolvable carrier through a liquid supply tube to an outlet of the tube;

means for establishing an electric field between the outlet and a support surface spaced from the outlet to cause liquid issuing from the outlet to form at least one fiber [fibre] or fibrils of the biodissolvable carrier;

means for causing the fiber [fibre] or fibrils to deposit onto the support surface to form a fiber web or mat;

means for forming from the fiber web or mat [to form] a plurality of individual tablets [each comprising a fibre web or mat]; and

means for incorporating at least one active ingredient into the web or mat, the individual tablets being configured to melt, liquefy, disintegrate or dissolve in a wet environment.

20. (Once amended) Apparatus according to claim [17, 18 or] 19, [further comprising, for providing] wherein the liquid [,] is a supply selected from a group consisting of a gelatin, starch, cellulose, a cellulose derivative, a water soluble polymer, [such as] polyvinyl pyrrolidone, polyvinyl alcohol, poly-sucrose, a sugar.
21. (Once amended) Apparatus according to claim [any one of claims 17 to] 19, [further comprising, as] wherein the liquid [,] is a supply selected from a group consisting of a solution consisting essentially of 5 grams of gelatin in 7 to 9 milliliters [millilitres] of water and 10 to 11 milliliters [millilitres] of ethanol.

22. (Once amended) Apparatus according to claim [any one of claims 17 to] 19, [further comprising, as] wherein the liquid [,] is a supply of a solution consisting essentially of 5 grams of gelatin in 8 milliliters [millilitres] of water, 10 milliliters [millilitres] of ethanol and 1 milliliter [millilitre] of peppermint flavoring [flavouring].
23. (Once amended) Apparatus according to claim 19, [any one of claims 17 to 22,] further comprising air flow causing means for facilitating the deposition of the at least one fiber [fibre] or fibrils onto the support.
24. (Once amended) Apparatus according to claim 19, [any one of claims 17 to 23,] wherein the electric field establishing means comprises means for applying a positive potential to the support.
25. (Once amended) Apparatus according to claim 19, [any one of claims 17 to 24,] further comprising a rotatable endless surface as the support.
26. (Once amended) Apparatus according to claim 19, [any one of claims 17 to 25,] further comprising an environmental control means for regulating the temperature of the region where liquid issues from the outlet.

2. 3. 4. 5. 6. 7. 8. 9. 10. 11. 12. 13. 14. 15. 16. 17. 18. 19. 20. 21. 22. 23. 24. 25. 26. 27. 28. 29. 30. 31.
27. (Once amended) Apparatus according to claim 19, [any one of claims 17 to 26,] further comprising spraying means for spraying the at least one active ingredient onto at least one of: the fiber [fibre] or fibrils; the mat or web; and individual tablets.
28. (Once amended) Apparatus according to claim 19, [any one of claims 17 to 27,] further comprising means for supplying the active ingredient so that the at least one fiber [fibre] or fibrils have a core containing the active ingredient.
29. (Once amended) A consumable or dissolvable tablet, pad or mat manufactured using a method in accordance with claim 34. [any one of claims 1 to 16 or apparatus in accordance with any one of claims 17 to 28.]
30. (Once amended) A consumable or dissolvable tablet produced by subjecting liquid comprising the carrier material to a high electric field and comprising a web of fibers [fibres] of a [biodissolvable] carrier material carrying at least one active ingredient, the carrier material being configured and arranged to melt, liquefy, dissolve or disintegrate in a wet environment [such as on the tongue or in the mouth of a human being or other animal].
31. (Once amended) A consumable or dissolvable tablet [comprising a] of claim 30, wherein the web of fibers [fibres] or fibrils are of gelatin, [produced by subjecting] the liquid comprising gelatin, [to a high electric field and carrying at least one active

ingredient, the tablet being arranged to dissolve or disintegrate in a wet environment such as on the tongue or in the mouth of a human being or other animal.]

32. (Once amended) A tablet according to claim 30, [claims 29, 30 or 31] wherein the active ingredient comprises a pharmacologically or biologically active ingredient.

* * * * *

10/018160
PROMPT Rec'd 01 NOV 2001
PCT/GB00/01728

A METHOD AND APPARATUS FOR MANUFACTURING
DISSOLVABLE TABLETS

This invention relates to a method and apparatus for
5 manufacturing dissolvable tablets especially, but not
exclusively, dissolvable tablets carrying at least one
pharmacologically or biologically active ingredient for
therapeutic or prophylactic treatment of an animal such
as a human being.

10 Conventional medicines to be ingested in a solid
form are manufactured as a compressed solid tablet or a
capsule containing granules which when swallowed enter
into the blood stream via the gastro-intestinal tract.
Some patients have, however, difficulty in swallowing
15 tablets or capsules. To address this problem and/or to
cause the active ingredient to dissolve at the oral
mucosa so that it enters the blood stream without
entering the gastro intestinal tract, tablets or pills
that dissolve on the tongue or in the mouth have been
20 manufactured. This enables buccal delivery of drugs which
is especially advantageous where the drug is intended to
be delivered to the central nervous system because it
enables rapid delivery of the drug to the brain and
avoids or at least inhibits delivery of the drug to the
25 non-targetted areas such as the gastro-intestinal tract
where the presence of the drug may have disadvantageous
side effects. Also, drug absorption through the blood-
rich epithelium in the mouth, rather than the chemically

hostile environment of the stomach and the intestine may generally be advantageous.

Such quick dissolving tablets are conventionally formed by dissolving food or pharmacological grade gelatin to form a gelatin solution. The gelatin solution is then frozen solid converting the water content into ice. The unbound ice is then removed under conditions of low pressure which cause the ice crystals to sublime, turning them directly into water vapour which is collected by a water vapour condenser. The vacuum encourages the orderly migration of water vapour to the condenser and so as to assure that the pressure of the water vapour remains below its triple point as is required for sublimation to occur. Secondary drying is then required to remove the tightly bound (sorbed) water that is strongly attached to the protein molecules. This tightly bound water is difficult to remove because it has a lower vapour pressure than free liquid at the same temperature. Accordingly this secondary drying is a slow process.

The initial rigid ice matrix of the frozen sample and the exceptionally gentle drying ensure that the dried resulting product maintains its structural integrity.

The above described process results in tablets or pills that regularly dissolve or disintegrate in the mouth or on the tongue. However, the process described above is a relatively complex process and generally has to be carried out as a batch-by-batch process.

It is the aim of the present invention to provide apparatus for and a method of manufacturing dissolvable tablets that may dissolve or disintegrate rapidly in the mouth, on the tongue or on any wet surface or in a wet environment, suitable for continuous mass production.

In one aspect, the present invention provides a method of manufacturing dissolvable tablets which comprises using electrohydrodynamic comminution to form a plurality of individual tablets or pills, with each 10 tablet consisting of a fibre web or mat which will dissolve or disintegrate on the tongue or in the mouth of a consumer such as a patient.

The tablets or pills may carry an active ingredient which may be, for example, a drug or other therapeutic agent. The active ingredient may be: carried by (for 15 example in solution with) the liquid or molten material used to form the fibres; provided by electrostatically coating the mat or individual tablets or pills with charged particles; provided by providing the fibres as 20 cored fibres with the core containing the active ingredient; or provided by spraying the fibres after or during deposition with oppositely charged particles of the active ingredient so as to form alternate layers of fibres and the active ingredient. One or more of these 25 techniques may be used to form a particular tablet and different active ingredients may be incorporated into the same tablet. For example, where the tablets are formed by a sandwich of alternate layers of fibres and the active ingredient, the composition of the different layers of

active ingredients may be different. In addition, the composition of the fibres forming each of the layers of fibres may be different. This would allow, for example, controlled release of different active ingredients 5 enabling, for example, buccal delivery of a first active ingredient and then later delivery in the gastro-intestinal tract of the same or a different active ingredient, so enabling, for example, sustained or controlled delivery of a drug or other active ingredient 10 or controlled multiple drug therapy.

A method embodying the invention should enable accurate doses of an active ingredient such as a drug to be delivered to any wet surface in a form which is easy and convenient to handle, for example: the application of 15 a growth factor or other compound to an open wound where a pad or tablet would quickly dissolve and release an even distribution of an active ingredient to the surface of the wound; or the delivery of a local anaesthetic to an eye ball after surgery; or delivery of drugs to any 20 animal; or even reconstitution of a dried drug for dissolution in water such as for injection, drinking or eating with food.

The fibres may be formed using any suitable biologically acceptable or compatible polymer that is 25 hydrophilic so that, on contact with a wet surface, it effectively deliquesces becoming liquid by absorbing the water, thereby dissolving. Suitable such polymers include food grade gelatins, polyvinyl pyridine, polyvinyl alcohol, polysucrose, other polysaccharides such as

starch and cellulose and its derivatives, sugars and confectionary mixtures such as toffee and caramel and any other biologically compatible products that can be formulated into a liquid solution suitable for use in the 5 electrohydrodynamic comminution process or can be made liquid by the application of heat.

Embodiments of the present invention will now be described, by way of example, with reference to the 10 accompanying drawings in which:

Figure 1 shows a part sectional very schematic side view of apparatus embodying the invention;

Figure 2 shows a part sectional view taken along the line II-II in Figure 1;

15 Figure 3 shows a very schematic part sectional view of a modified form of the apparatus shown in Figure 1;

Figure 4 shows very schematically a further modification of the apparatus shown in Figure 1;

20 Figure 5 shows a part sectional very diagrammatic view of a further modification of the apparatus;

Figure 6 shows diagrammatically a modified form of comminution arrangement for use in the apparatus shown in any of Figures 1 to 5;

Figures 7 to 9 show electronmicrographs with Figures 25 7 and 8 illustrating the structure of a tablet produced by the conventional freeze gelling technique and Figure 9 illustrating the structure of a tablet produced using a method embodying the present invention.

Referring now to the drawings, the apparatus 1 shown in Figure 1 consists of a container 2 made of thermally insulative material such as a glass, or a plastics material such as Perspex (trade mark).

5 A comminution arrangement 3 is mounted within the chamber 2. The comminution arrangement 3 comprises a hollow tube 4 having an outlet nozzle 4'. The tube 4 is electrically conductive at least adjacent its nozzle 4'. The electrically conductive nozzle 4' is coupled to the 10 earth terminal E of a high voltage source or supply 5 mounted outside the chamber 2. The high voltage terminal 5a of the high voltage supply 5 is coupled to a corona discharge electrode 50 for charging a support surface 6 disposed opposite the outlet nozzle 4a so as to enable an 15 electric field to be established between the nozzle 4a and the support surface 6. Other ways of charging the support surface 6 such as a brush contact may be used, but the use of a corona discharge electrode 50 has the advantage of avoiding arcing and subsequent erosion.

20 The support surface 6 is in the form of a conveyor belt supported along its length (see Figure 2) by rollers 60 rotably mounted to supports (not shown) such that, as shown most clearly by Figure 2, the conveyor belt 6 extends at an angle to the horizontal. One of the 25 rollers 60 is fixedly mounted to the spindle 7a of a drive motor 7 mounted outside the chamber 2.

As shown in Figure 2, the conveyor belt extends through an aperture 2a provided in the chamber 2. To maintain the environment within the chamber 2a and to

assist in formation of the tablets as will be described below, the aperture 2a has flexible lips 20 formed of a rubber or plastics material which press onto the surface of the conveyor belt 6. An environmental control unit 8 5 may be mounted within the chamber so as to directly enable control of the temperature of the air in the region 40 where liquid issuing from the nozzle 4a is subject to the electric field established between the nozzle 4a and the support surface 6.

10 A perforate wall 2b of the chamber 2 separates the main chamber from a subsidiary chamber 2c which houses an exhaust pump 14. The exhaust pump 14 has an outlet 14a for exhausting air to the outside of the chamber 2.

15 A biologically acceptable carrier liquid is supplied to the tube 4 from a liquid supply reservoir 9 mounted outside the chamber 2 by means of a pump 10. The temperature of the reservoir 9 may be controlled so that its contents are thermally adjusted to produce fibres when sprayed. For example a solid may be heated to a 20 liquid state ("melt") to be sprayed, or an inviscid liquid may be cooled to make it more viscous. In this way the range of products and formulations that can be sprayed may be extended beyond liquids that are sprayable at room temperature and may avoid the need for solvents.

25 As shown in Figure 2 a horizontal further conveyor belt 6' is supported on rollers 60 adjacent the conveyor belt 6 so that in known manner material can pass directly from the conveyor belt 6 to the conveyor belt 6'. A cutting device 11 is mounted above the further conveyor

belt 6' outside of the chamber 2 so that a matrix of cutting blades 11a of the cutting device are moveable towards and away from the conveyor belt. A hopper 12 is mounted beneath the end of the conveyor belt to receive
5 the resulting tablets or pills.

As shown in Figure 2, a spraying device 13 may be provided at the end of the further conveyor belt to spray the resulting tablets with a final coating as will be explained below.

10 In use of the apparatus shown in Figure 1, the high voltage 5 is first switched on to establish an electric field between the nozzle 4' and the support surface 6. Typically, the high voltage applied to the support surface or spindle 6 will be approximately 20 kilovolts.
15 Applying the high voltage to the support surface 6 and earthing the nozzle 4' acts to focus the electric field and produce less erratic spraying than would sometimes be produced if the high voltage was applied to the nozzle 4' and the surface 6 was earthed. The drive motor 7 and pump
20 14 are then activated so as to rotate or drive the conveyor belt 6'. If required, as environmental control unit 8 may be used to adjust the ambient temperature so that either warm or cold air, dried or humidified flows through the chamber 2. The temperature of the air within
25 the chamber 2 will be controlled to be appropriate for the formulation being sprayed. For example, the temperature may be controlled to have a value between 0°C and 200°C, depending on the formulation being sprayed. The temperature may, depending upon the formulation being

sprayed, be in the range of 30°C to 200°C or 50°C to 100°C.

The liquid pump 10 is then activated to pump liquid to the tube at a rate of between 1 and 20ml, for example 5 about 4ml (millilitres), per hour.

Liquid issuing from the output nozzle 4' forms, under the influence of the applied electric field, a Taylor cone and jet which solidifies to form a fibre which is attracted to and deposits on the support surface 10 6 as a fibrous web or mat. The speed of movement of the conveyor belt 6 is typically less than 1 metre/second (ms^{-1}). A conveyor belt 1 metre wide moving at 5mm/s or 0.005 m/s should enable 100,000 tablets with a surface area of 2cm² to be produced per hour.

15 The mat or web is moved away from the area of the high electric field by the conveyor belt, is squeezed slightly against the conveyor belt 6 by the resilient lips 20 which act to compress the fibre mat or web slightly and then transferred to the further conveyor 20 belt 6'.

The cutting device 11 is reciprocated towards and away from the further conveyor belt 6' by conventional reciprocating means (not shown) in synchronism with the movement of the belt so that the cutting blades 11a of 25 the cutting device cut the compressed mat or web into tablets or pills 30. Although not shown, a printing stage may be provided for printing information such as a logo or dosage amount on the tablets. The tablets or pills 30

then drop off the end of the further conveyor belt 6' and are collected in the hopper 12.

As noted above, a spraying device 13 may be provided to coat the individual tablets or pills 30 with, for example, a sugar coating. The spraying device 13 may be a conventional spraying device or may be an electrohydrodynamic spraying device of the same type as the comminution arrangement 3.

Typically the gap between the outlet nozzle 4 and the support surface 6 is about 1 to 20 cm.

The use of the conveyor belt arrangement enables a continuous process and also allows the highly charged fibre web or mat to be moved away from the area of the electric field leaving a more appealing lower charged surface behind to facilitate the deposition of further material. In the arrangement described above, the nozzle 4' is arranged to spray horizontally onto the conveyor belt 6 which is arranged at an angle to the horizontal. This has the advantage that any undesired large or satellite droplets issuing from the nozzle 4' will, due to the influence of gravity, fall away from both the nozzle 4' and the conveyor belt 6. Where the possibility of satellite droplets is small and does not present a problem then the conveyor belt 6 may extend horizontally and the nozzle 4' may be arranged above or below the conveyor belt 6 so as to spray directly downwardly or upwardly, respectively, onto the conveyor belt 6.

The liquid supplied to the tube 4 may contain a pharmacologically or biologically active ingredient such

as a drug or medicament to be imbibed by the patient, especially drugs acting upon the central nervous system where buccal delivery via the mouth mucosa will have specific benefits and/or where entry into the body via 5 the gastro-intestinal tract is to be minimised for physiological reasons, for example to inhibit adverse side effects. Examples of such drugs are eletriptan and sildenafil.

As an example, the biologically acceptable carrier 10 may be gelatin. Experiments to determine the optimum gelatin-based formulation for achieving a tablet which will maintain its shape but will dissolve or disintegrate readily on the tongue were carried out. These experiments were carried out using an annular nozzle 15 which, for convenience, was arranged to spray onto a slowly rotating (for example 1 revolution/hour) 350 mm diameter metal plate rather than onto the conveyor belt 6. The nozzle 4' was separated from the plate by a distance which was varied between 60 and 200 mm and a 20 voltage of between 25 and 30 kV was applied to the plate. Generally 30 kV was applied to the plate. The liquid to be sprayed to produce the desired tablets was supplied to the nozzle 4' with a flow rate between 10 and 20 ml per hour.

In this case, the liquid to be sprayed consisted of 25 CRODA spray dried fish gelatin with the solvent being a water-ethanol mix. In the experiments, formulations were investigated in which 5g of the fish gelatin was

dissolved in between 17 and 30 ml of the water-ethanol solvent.

It was found that the spray performance of the formulation was affected by the overall ratio of water to ethanol content and also by the overall viscosity of the solution. The ratio of water to ethanol was varied between 2:1 and 1:2. It was found that a higher ethanol content produces a more sprayable solution but that an excess of ethanol causes the gelatin to precipitate out of solution with it being impossible to properly dissolve the 5g of gelatin in an 8 ml water : 12 ml ethanol (2:3) solvent mix. It was also found that a high proportion of water provides a more stable solution that is more difficult to spray and also produces a slightly wetter product that is more likely to contain droplets in addition to the desired fibre. The best formulations were found to have a solvent consisting of 7 to 9 ml of water and 10 to 11 ml of ethanol. The current preferred formulation is 8 ml of water, 10 ml of ethanol, 1 ml of peppermint flavouring (which is a mixture of water and isopropanol plus the flavouring) and 5g of the spray dried fish gelatin.

The less viscous solutions (that is where there was 22 to 30 ml of solvent per 5g of fish gelatin) sprayed in a more stable fashion but tended to produce droplets and some beaded fibres. In contrast, more viscous solutions having 17 to 21 ml of the solvent produced the desired distinct fibres and resulted in tablets having only a little friability.

Increasing the distance between the nozzle 4' and the support surface onto which spraying was being effected increased the likelihood of fibre formation (because it allowed further time for evaporation of the solvent) and made the resultant tablet more fibrous and friable. In contrast, placing the nozzle 4' very close (60 to 70 mm) to the support surface had the opposite effect with the solvent having less chance to evaporate and thus encouraging a less friable but more dense product. As a result of these experiments, it was found that the optimum distance for spraying the current preferred formulation to achieve the desired low density low friability tablets was a separation of between 100 and 200 mm between the nozzle 4' and the plate with the actual distance within this range being fairly flexible.

The addition of sweeteners to increase the palatability of the tablet was investigated. It was found that the addition of a little (50 mg or so) of saccharine to the liquid resulted in no noticeable effect on the end tablet apart from the desired sweetness. Surprisingly, however, when a similar quantity of d-sorbitol (mannitol) was added, it was found that the tablets shrank catastrophically over a day or, so resulting in a high density rubber-like structure which would not dissolve readily in the mouth or on the tongue.

Other grades of gelatin may be used to adjust the physical properties of the product. For instance, a product made purely from fish gelatin dissolves extremely quickly in water but can also be dissolved by sweat on

the fingers. Although this problem can be countered by a thin coating applied to the finished pill or tablets, other less soluble gelatine grades may be used instead of, or as well, as the fish gelatin to make it more robust and less fryable. Also the degree of spray drying of the gelatin may affect the characteristics of the end product.

Further experiments have shown that many other formulations may be used which do not contain animal products and are therefore suitable for vegetarians. These will include alternative solutes such as polyvinyl pyridine, polyvinyl alcohol, poly-sucrose, other polysaccharides, such as starch and cellulose and its derivatives, sugars and confectionery mixtures, such as toffee and caramel, and other biologically compatible products that can be formulated into a liquid solution or made liquid through the application of heat and which will dissolve or melt on contact with wet surfaces as required. Mixtures of different polymers may also be used, for example a small quantity of another biologically acceptable polymer may be added to a gelatin formulation to improve its performance.

The following table gives specific examples of polymer formulations that may be used as the biologically acceptable carrier. In this table the flow rate column indicates the flow rate from the outlet of the supply tube, the voltage indicates the voltage difference between the outlet tube and the conveyor belt used to cause electrohydrodynamic spraying and the comments

column indicates the spray properties and characteristics of the resulting web or mat product. The separation is the distance of the supply tube outlet from the conveyor belt and "Mw" is the molecular weight.

5

| | Polymer | Formulation | Flow Rate | Voltage (kV) | Separation (at room temperature) | Comments |
|----|--|--|---------------|--------------|----------------------------------|--|
| 10 | "Luviskol" a vinylpyrrolidone/vinylacetate copolymer

Manufactured by BASF, 67056 Ludwigshafen Germany | Luviskol is provided as a 50% solid in ethanol solution. This in turn is diluted with extra ethanol in a ratio of two parts of Luviskol to one part of ethanol | upto 30 ml/hr | 15 kV | Wide range from 5cm to 15 cm | Very stable spray. Build up fairly rapid. Product very soluble. Large fibres. |
| 15 | Polyvinyl-pyrrolidone | Mw 360,000: 0.5g in 10ml ethanol | upto 20 ml/hr | 15 - 20kV | Wide range from 5cm to 15cm | Very stable. Not a very rapid build up of product |
| | Gelatin | 5g in: 8ml water, 12ml ethanol | upto 30 ml/hr | 20-30kV | Wide range from 5cm to 15cm | Not very stable. However rapid build up of web. Product is very soluble in water |

| Polymer | Formulation | Flow Rate | Voltage (kV) | Separation (at room temperature) | Comments |
|---|---|-----------|--------------|----------------------------------|--|
| Polyvinyl-alcohol | Mw 100,000 and 130,000. Concentration of 0.1g/ml in 1:1 water and ethanol | 10ml/hr | 14 - 20kV | 6 to 10cm | Very stable, very soluble in water. Lower molecular weights produce denser product, which is less soluble, and higher molecular weights are too viscous. |
| "Luvitec VPI 55"
vinylpyrrolidone/vinylimidazole copolymer

Manufactured by BASF | ~4g in 10ml ethanol | 5ml/hr | 12kV | 9cm | Multi-jets, very soluble loosely packed mat. Very tacky. Stable. Possible to make more concentrated. |

5
10

Figure 3 is a view similar to Figure 2 showing a modification of the arrangement shown in Figure 2. As can be seen from Figure 3, the apparatus 1a shown in Figure 3 differs from that shown in Figures 1 and 2 in that the sprayer 13 is provided within the chamber 2 and is arranged so as to direct a spray at liquid issuing from the nozzle 4a so that the fibre is coated as it is formed. Figure 3 also shows a spraying liquid reservoir 13a and pump 13b.

In the embodiments described above, the tablets or pills are formed using the cutting device 11. Different forms of cutting devices may, of course, be used. For

example, a pair of reciprocating knives may be provided one on either side of the conveyor belt each arranged to cut at an angle to the length of the conveyor belt so as to produce lozenge shaped tablets or a rolling blade may 5 be used. As another, possibility, a cutter defining a plurality of tablet or pill shapes may be used which is lowered onto the fibrous mat to cut an area of the fibrous mat into an array of pill or tablet shapes. By applying suction to the cutting device, the cut shapes 10 may then be lifted from the fibrous mat by the cutting device and transferred to and aligned with a blister pack base. Once the cutting device has been correctly positioned over the blister pack base, then the suction pressure may be reversed so as to blow the tablets gently 15 into respective receptacles in the blister pack base. This cutting device may be arranged to cut out the pills or tablets so that they have a circular or oval shape. To minimise wastage, the cutting device may, alternatively, be arranged to cut out the tablets so that 20 they have a rectangular or hexagonal shape with the corners of the rectangles or hexagons being rounded.

In the apparatus described above, the fibres are formed using a single cylindrical liquid supply tube 4 having an annular outlet nozzle 4'. However, the 25 apparatus may be provided with an array of such liquid supply tubes extending transversely of the direction of movement of the conveyor belt 6 or even with a matrix of such liquid supply tubes. Where such an array is used, then the separate liquid supply tubes each provide a

commminution site. In order to avoid interference effects between the separate comminution sites, the spray heads should be separated by a distance of at least 10 to 20 cm, or provided with electrostatic screening electrodes. Alternatively or additionally, a slot-like nozzle may be used.

In addition, or as an alternative, a number of liquid supply tubes may be arranged along the length of the conveyor belt. Typically, the spacing between liquid supply tubes in this longitudinal direction should be 20 to 40 cm, for example 30 cm, although they may be placed closer together if the individual liquid supply tubes are electrostatically screened. Figure 4 illustrates very diagrammatically a modification of the apparatus shown in Figures 1 and 2 wherein nine liquid supply tubes 4a to 4i are arranged so as to extend along the length of the conveyor belt 6. As shown in Figure 4, each liquid supply tube is connected to a respective liquid supply pipe 10a to 10i to which liquid is pumped via a corresponding pump (not shown) from a corresponding reservoir (not shown). Thus, each of the liquid supply tubes 4a to 4i will be coupled via a liquid supply pipe and pump to a reservoir in the manner similar to that shown in Figure 1 for the liquid supply tube 4.

Providing a plurality of liquid supply tubes along the length of the conveyer belt has a number of advantages. In particular, it enables different liquids to be supplied via the different liquid supply tubes 4a to 4i. As one example, alternate liquid supply tubes 4a,

4c, 4e and 4g may supply the polymer liquid formulation discussed above while the intervening liquid supply tubes 4b, 4d, 4f and 4h may supply a tacky ingredient such as gum arabic or gum tragacanth to facilitate adhesion of 5 the fibres to one another and the final liquid supply tube 4i may supply a flavouring or sugar coating. Also, the use of a plurality of nozzles supplying different liquids enables, for example, active ingredients which are lipophilic as opposed to hydrophilic to be 10 incorporated into the tablets.

To further facilitate adhesion of the fibres to one another and to make the resulting product less fluffy, if required, the nozzles of alternate liquid supply tubes may be charged to opposite polarities. In addition, one 15 or more of the liquid supply tubes 4a to 4i may be replaced by a spraying device which sprays charged dry powder of the opposite polarity to the fibres so that the dry powder is attracted to and sticks to the fibre. Such a dry powder may contain an active ingredient or 20 ingredients for the tablet and/or flavourings or colorings. One advantageous way of producing such electrically charged dry powder would be to use the triboelectric charging process. Another way would be to use ionic bombardment. Both these techniques are well 25 known. The ionic bombardment process provides a copious supply of ions which are attracted directly to the fibres and may be desirable in order to reduce the charge on the sprayed mat.

Typically, it is possible to achieve charge of the order of 1 coulomb per kilogram when producing the fibres from liquid but charge of only the order of 10^{-3} coulombs per kilogram for dry powder. Thus, if the dry powder is produced to be of the opposite polarity from the fibres, then the overall mat before separation into the tablets will still be charged to the polarity of the fibres but will have an overall reduced charge. This enables a large amount of oppositely charged particles to be applied to the spray mat.

In an embodiment, the liquid supply tubes arranged along the length of the conveyor belt may be arranged so as to provide, alternately, a supply of fibres and a supply of an active ingredient with opposite plurality voltages being applied to longitudinally adjacent liquid supply tubes so that a layer of fibres of one polarity is deposited followed by a layer of active ingredient of the opposite polarity followed by a layer of fibres of the one polarity followed by a layer of active ingredient of the other polarity and so on to the desired thickness. Different active ingredients may be provided in the different active ingredient layers and different fibres or fibre thicknesses may be provided in the different fibre layers. This may allow, for example, a multiple therapy tablet to be produced which enables, for example, rapid buccal delivery of one active ingredient and slower delivery via the gastro intestinal tract of the same or a different active ingredient.

As described above, an environmental control unit may be provided to control temperature and/or humidity. Where a plurality of liquid supply tubes spaced apart along the length of the conveyor belt are provided then 5 each liquid supply tube may be provided with its own local environmental control unit which may be provided, for example, immediately downstream of the liquid supply tube to allow, for example, for drying of the just-formed layer prior to deposition of further material on that 10 layer.

Another way of electrically compacting the product is to apply alternating polarities to the spray nozzles over time. The frequency would typically be quite low so the electrohydrodynamic process has time to adjust. 15 Frequencies below 10Hz are preferable.

Figure 5 illustrates very diagrammatically a further modification of the apparatus described above. In this example, the conveyor belt 6 is horizontally arranged, but the further conveyor belt 6' and the cutting device 20 11 are omitted and a field controlling arrangement is provided so as to direct the fibres only towards certain areas of the surface 6. As shown, this is achieved by provided on the surface of the conveyor belt 6 a tray-like arrangement 16 having a regular array of tablet or 25 pill sized and shaped recesses 16. The tray-like arrangement is designed so that the interior surface of each recess 16b is positively charged while the islands 16a between the recesses are negatively charged.

In this arrangement, the nozzle 4' is arranged to be negatively charged and the belt earthed by the high voltage source 5 so that the material issuing from the nozzle is negatively charged and thus will be attracted 5 into the recesses 16b but repelled from the islands 16a so that a series of individual tablet sized mats or webs of fibres are produced. Where non-gelatinous products are used the spray distance can be much reduced to around 1 to 2cm, and in such cases the nozzle can be placed just 10 above, making it easier to direct the spray into the well.

Figure 6 illustrates that schematically a further modification which may be made to the comminution arrangement 3. The arrangement 3a shown in Figure 6 has 15 two reservoirs 9a and 9b containing different liquids each coupled by a respective valve V1 and V3, a respective pump 10a and 10b and a further valve DV and V4 to a respective outlet nozzle 4'1 and 4'2. This arrangement enables a first liquid to be provided within 20 a curtain of the second liquid enabling a cord or coated fibre to be produced. It would be appreciated that Figure 6 is only very schematic. Further details of an arrangement for enabling a first liquid to be supplied within a second liquid are described in WO 98/03267 (see 25 especially Figures 11 and 14) the whole contents of which are hereby incorporated by reference.

Figures 7 to 9 are electronmicrographs showing in Figures 7 and 8 the structure of a conventional freeze dried tablet and in Figure 9 the mat or web like fibre

structure of a tablet produced using the apparatus shown in Figures 1 and 2 and the gelatin solution mentioned above. As can be seen, the resulting fibre consists of a fine mat or web of strains or fibres which appear to be simply individual strands of rapidly dried polypeptide chains that have become entangled to form strands or fibrils. These in turn would appear to have become entangled with one another forming strings which themselves become intertwined to form rope like structures which overlay one another to form a fibrous cotton wool like material. This very open fibre structure can be fully hydrolysed in the mouth with full breakdown of the secondary structure so that the fibres become disentangled but will not form junctions zones which would result in gelling of the product which would be undesirable.

The active ingredient or ingredients to be supplied by consumption of a tablet or pill produced using the apparatus described above may be any agent or substance which provides a desired effect in the consumer. For example, the active ingredient may be a medicament for use in the treatment by way of therapy, surgery or diagnosis or otherwise to improve quality of life of a human being or other animals. For example, the active ingredient may be nicotine, morphine, a vitamin, an antiseptic, an anti-inflammatory, an antibiotic, an anti-cancer agent or other pharmaceutical product, a vaccine, a protein, or an enzyme.

The present invention also has applications outside the medical field. Thus, the apparatus described above may be used to produce confectionary products which melt in the mouth. In such cases, the active ingredients may 5 comprise at least one or more of the following: a flavouring; chocolate; a colorant; and a sweetener.

The fibres may be formed using any suitable biologically acceptable or compatible polymer that is hydrophilic so that, on contact with a wet surface, it 10 effectively deliquesces becoming liquid by absorbing the water, thereby dissolving. Suitable such polymers include food grade gelatins, polyvinyl pyridine, polyvinyl alcohol, polysucrose, other polysaccharides such as starch and cellulose and its derivatives, sugars and 15 confectionary mixtures such as toffee and caramel and any other biologically compatible products that can be formulated into a liquid solution suitable for use in the electrohydrodynamic comminution process or can be made liquid to the application of heat.

20 As used herein the term "biodissolvable" means capable of being dissolved or disintegrated in the mouth or on the tongue of a human being or other animal and on another wet surface such as an open wound where the pad or tablet would dissolve quickly to release a drug or 25 other product onto the surface of the wound or an eye ball surface to deliver for example, a local anaesthetic to the eye ball after surgery. Tablets manufactured by a method in accordance with the invention may also be

provided so as to be reconstituted in water for injection or drinking or eating with food for example.

Other modifications will be apparent to the skilled person in the art.

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ARTICLE 34

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CLAIMS:

1. A method of manufacturing consumable or dissolvable tablets, comprising:
 - 5 supplying a liquid containing a biodissolvable carrier along a supply tube to an outlet of the tube;
 - 10 establishing an electric field between the outlet and a support surface spaced from the outlet to cause liquid issuing from the outlet to form at least one fibre or fibrils of the biodissolvable carrier which fibre or fibrils deposit(s) onto the support surface to form a fibre web or mat;
 - 15 separating the web or mat into a plurality of individual tablets; and
 - 20 incorporating at least one active ingredient in and/or the tablets.
2. A method according to claim 1, which comprising:
 - 25 separating the web or mat into a plurality of individual tablets by cutting the web or mat.
3. A method of manufacturing tablets, comprising:
 - 30 supplying through a supply tube to an outlet a liquid containing a hydrophilic biologically compatible carrier;
 - establishing an electric field between the outlet and a support surface spaced from the outlet to cause liquid issuing from the outlet to form at least one fibre or fibrils of the carrier;
 - causing the at least one fibre or fibrils to deposit onto the support surface to form a plurality of individual tablets each comprising a fibre web or mat which melts or liquifies on contact with a wet surface; and

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providing the tablets with at least one active ingredient.

5. A method according to any one of the proceeding claims, which comprises supplying to provide the liquid a composition comprising at least one of a gelatin, starch, cellulose, a cellulose derivative, a water-soluble polymer such as polyvinyl pyrrolidone, polyvinyl alcohol, poly-sucrose, a sugar.
10. 5. A method according to any one of claims 1 to 3, which comprises supplying as the liquid a solution consisting essentially of 5 grams of fish gelatin in a solvent consisting of from 7 to 9 millilitres of water and 10 to 11 millilitres of ethanol.
15. 6. A method according to any one of claims 1 to 3, which comprises supplying as the liquid a solution consisting essentially of 5 grams of fish gelatin in a solvent consisting of 8 millilitres of water, 10 millilitres of ethanol and 1 millilitre of peppermint flavouring.
20. 7. A method according to any one of the preceding claims, which comprising providing an air flow to encourage the deposition of the at least one fibre or fibrils on the surface.
25. 8. A method according to any one of the preceding claims, which further comprises regulating the temperature, for example by applying heat, of the region where the liquid issues from the outlet to facilitate the formation of the at least one fibre or fibrils.

9. A method according to any one of the preceding claims, which comprises establishing the electric field by applying a high voltage to the surface.
- 5 10. A method of manufacturing tablets, comprising:
supplying a liquid consisting essentially of a hydrophilic solution of gelatin through a liquid supply tube to an outlet of the tube;
establishing an electric field between the outlet
10 and a support surface spaced from the outlet to cause liquid issuing from the outlet to form on the support surface a web or mat consisting of at least one gelatin fibre or gelatin fibrils;
separating the web or mat into a plurality of
15 individual tablets; and
incorporating at least one active ingredient and a sweetener such as saccharine into and/or on the tablets.
- 20 11. A method according to any one of the preceding claims, which comprises using as the surface a rotatable endless surface such as a belt.
- 25 12. A method according to any one of the preceding claims, which comprises incorporating the at least one active ingredient by spraying the active ingredient onto at least one of: the at least one fibre or fibrils; the mat or web; and the individual tablets.
- 30 13. A method according to any one of the preceding claims, which comprises incorporating the active ingredient into the at least one fibre or fibrils.
- 35 14. A method according to any one of the preceding claims, which comprises forming the at least one fibre of fibrils with a core containing an active ingredient.

15. A method of manufacturing a pharmaceutical product which comprises using a method in accordance with any one of the preceding claims and providing as the at least one active ingredient an ingredient which is
5 pharmacologically or biologically active.

16. A method of manufacturing a confectionary product which comprises using a method in accordance with any one of claims 1 to 14 to form a plurality of individual tablets and incorporating as the at least one active ingredient at least one of the following: sugar;
10 chocolate; a flavouring; and a colorant.

17. Apparatus for manufacturing consumable or
15 dissolvable tablets, comprising:

means for supplying a liquid containing a biodissolvable carrier through a liquid supply tube to an outlet of the tube;

means for establishing an electric field between the
20 outlet and a support surface spaced from the outlet to cause liquid issuing from the outlet to form at least one fibre or fibrils of the biodissolvable carrier which deposit(s) onto the support surface to form a fibre web or mat;

25 means for separating the web or mat into a plurality of individual tablets; and

means for incorporating at least one active ingredient in the tablet.

30 18. Apparatus according to claim 15, wherein the separating means comprises at least one cutter.

19. Apparatus for manufacturing consumable or dissolvable tablets, comprising:

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- means for supplying a liquid containing a biodissolvable carrier through a liquid supply tube to an outlet of the tube;
- 5 means for establishing an electric field between the outlet and a support surface spaced from the outlet to cause liquid issuing from the outlet to form at least one fibre or fibrils of the biodissolvable carrier;
- 10 means for causing the fibre or fibrils to deposit onto the support surface to form a plurality of individual tablets each comprising a fibre web or mat; and
- means for incorporating at least one active ingredient into the web or mat.
- 15 20. Apparatus according to claim 17, 18 or 19, further comprising, for providing the liquid, a supply of a gelatin, starch, cellulose, a cellulose derivative, a water soluble polymer such as polyvinyl pyrrolidone, polyvinyl alcohol, poly-sucrose, a sugar.
- 20 21. Apparatus according to any one of claims 17 to 19, further comprising, as the liquid, a supply of a solution consisting essentially of 5 grams of gelatin in 7 to 9 millilitres of water and 10 to 11 millilitres of ethanol.
- 25 22. Apparatus according to any one of claims 17 to 19, further comprising, as the liquid, a supply of a solution consisting essentially of 5 grams of gelatin in 8 millilitres of water, 10 millilitres of ethanol and 1 millilitre of peppermint flavouring.
- 30 23. Apparatus according to any one of claims 17 to 22, further comprising air flow causing means for facilitating the deposition of the at least one fibre or fibrils onto the support.

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24. Apparatus according to any one of claims 17 to 23, wherein the electric field establishing means comprises means for applying a positive potential to the support.
- 5 25. Apparatus according to any one of claims 17 to 24, further comprising a rotatable endless surface as the support.
- 10 26. Apparatus according to any one of claims 17 to 25, further comprising an environmental control means for regulating the temperature of the region where liquid issues from the outlet.
- 15 27. Apparatus according to any one of claims 17 to 26, further comprising spraying means for spraying the at least one active ingredient onto at least one of: the fibre or fibrils; the mat or web; and individual tablets.
- 20 28. Apparatus according to any one of claims 17 to 27, further comprising means for supplying the active ingredient so that the at least one fibre or fibrils have a core containing the active ingredient.
- 25 29. A consumable or dissolvable tablet, pad or mat manufactured using a method in accordance with any one of claims 1 to 16 or apparatus in accordance with any one of claims 17 to 28.
- 30 30. A consumable or dissolvable tablet produced by subjecting liquid comprising the carrier material to a high electric field and comprising a web of fibres of a biodissolvable carrier material carrying at least one active ingredient, the carrier material being arranged to dissolve or disintegrate in a wet environment such as on

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the tongue or in the mouth of a human being or other animal.

31. A consumable or dissolvable tablet comprising a web
5 of fibres or fibrils of gelatin produced by subjecting
 liquid comprising gelatin to a high electric field and
 carrying at least one active ingredient, the tablet being
 arranged to dissolve or disintegrate in a wet environment
 such as on the tongue or in the mouth of a human being or
10 other animal.

32. A tablet according to claims 29, 30 or 31, wherein
the active ingredient comprises a pharmacologically or
biologically active ingredient.

15 33. Use of electrohydrodynamic comminution to produce a
 consumable or dissolvable tablet.

ABSTRACT OF THE DISCLOSURE

Consumable or dissolvable tablets are manufactured by supplying a liquid containing a biodissolvable carrier to an outlet; establishing an electric field between the outlet and a support surface to cause liquid issuing from the outlet to form at least one fiber or fibrils of the biodissolvable carrier which fiber or fibrils deposit(s) onto the surface to form a fiber web or mat; separating the web or mat into a plurality of individual tablets; and incorporating at least one active ingredient on or in the tablets.

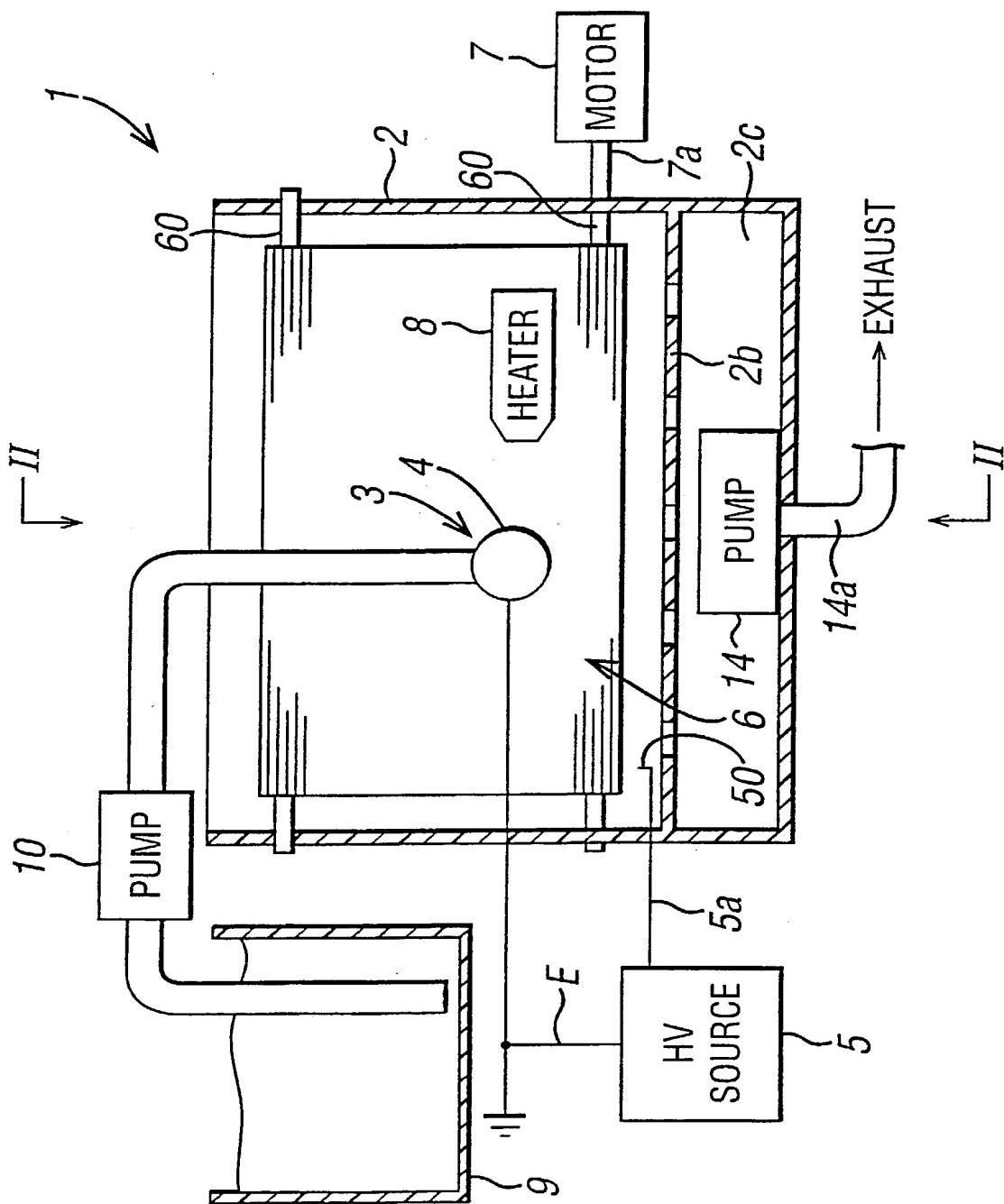
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FIG. 1



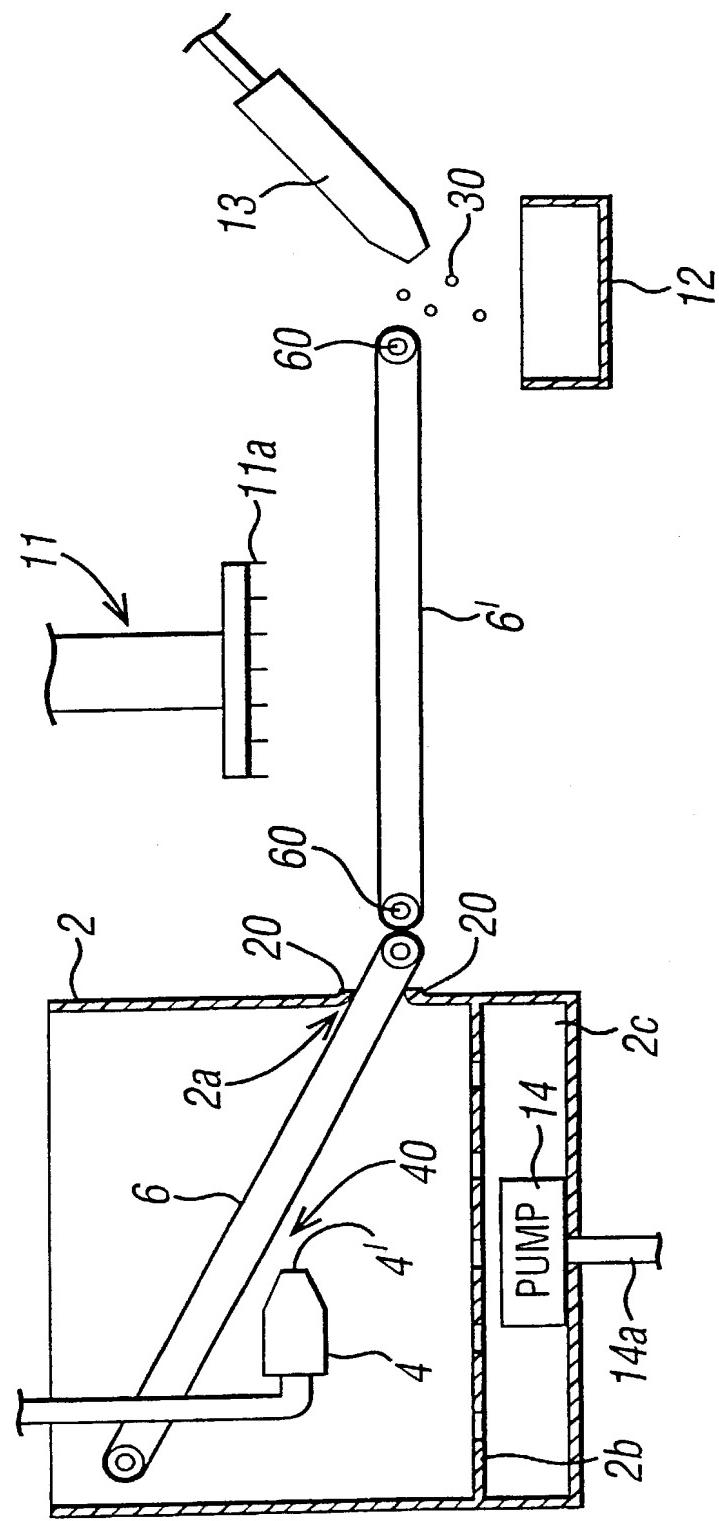
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FIG. 2

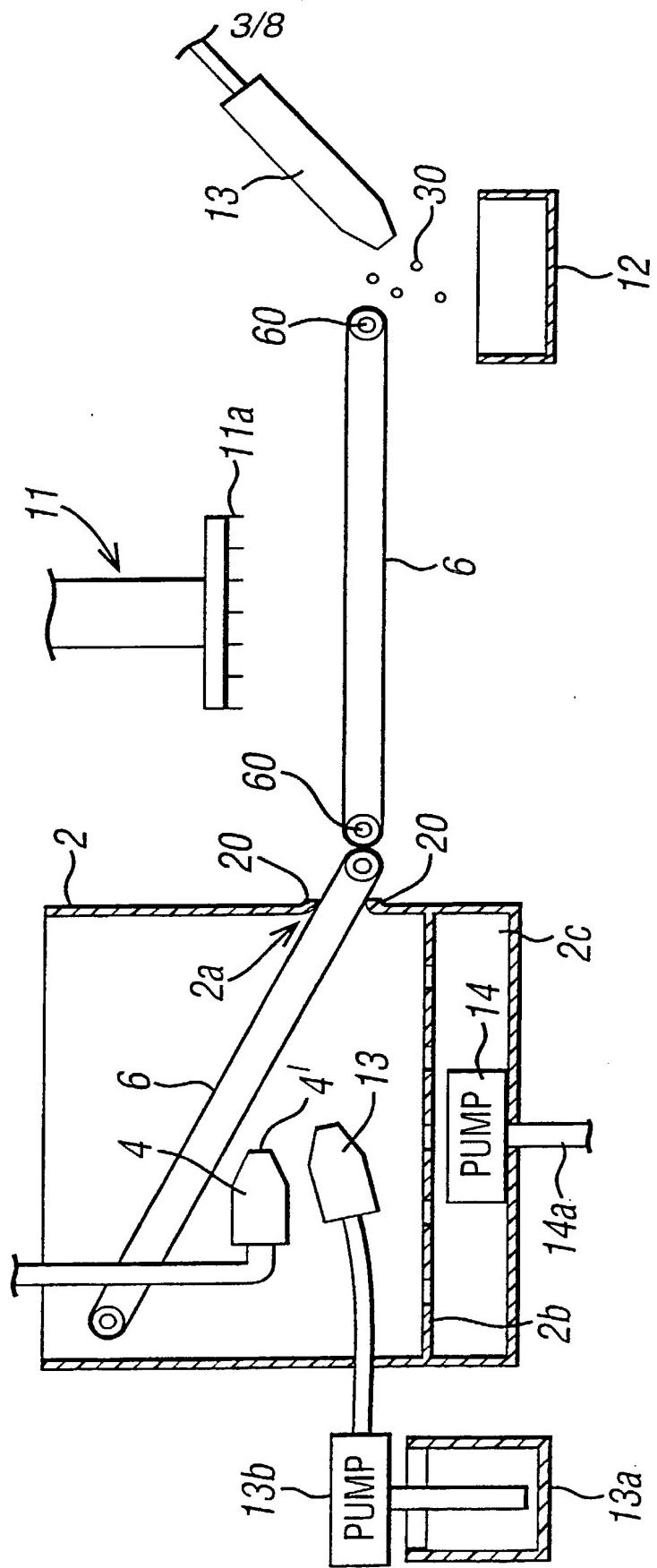


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FIG. 3



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FIG. 4

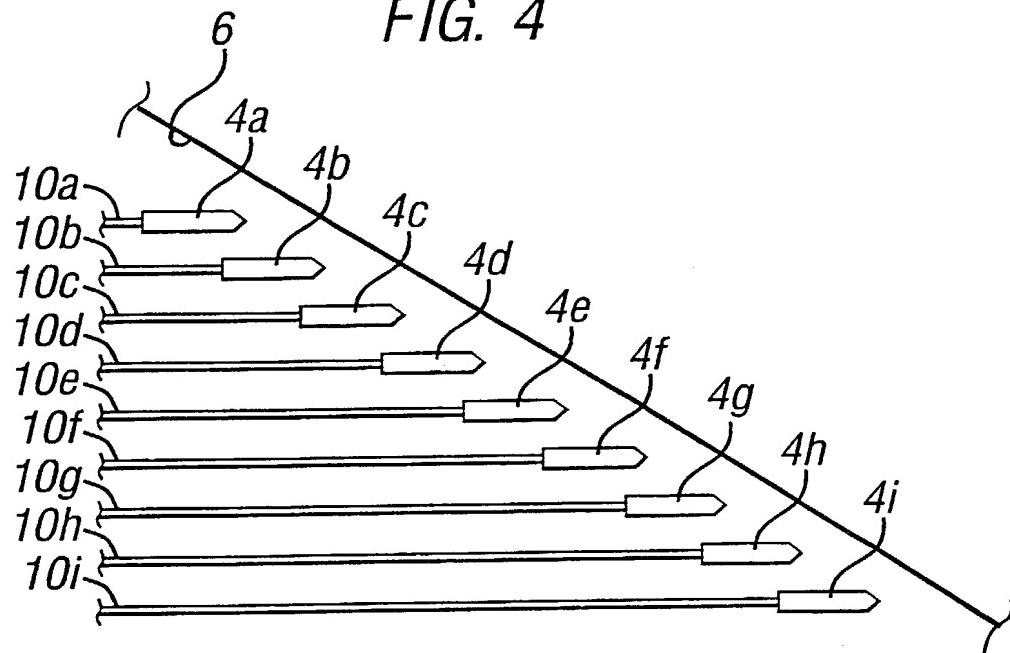
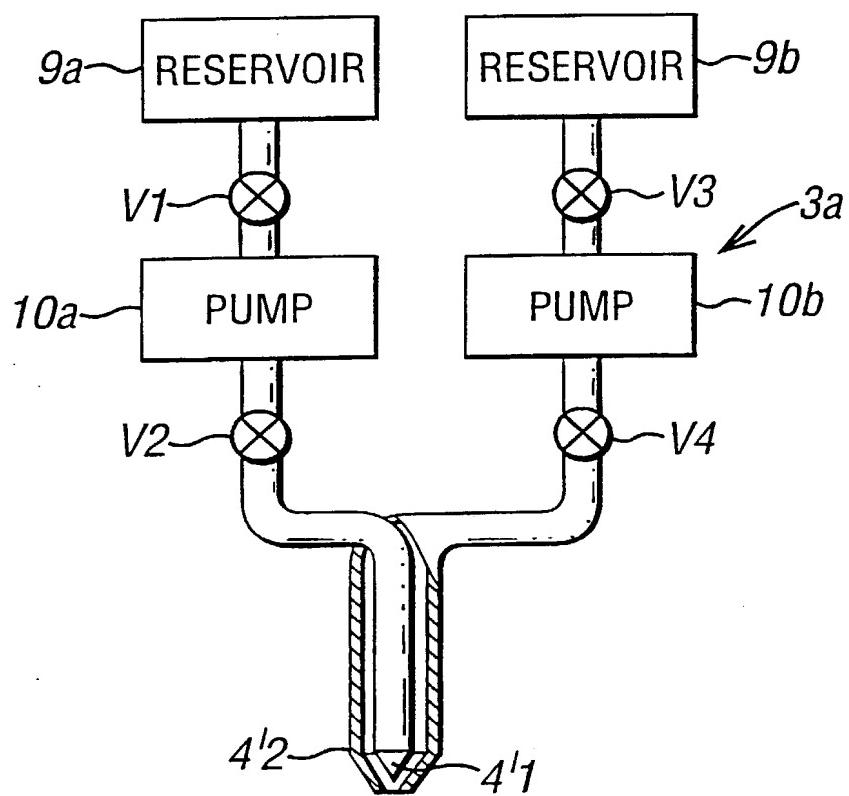


FIG. 6



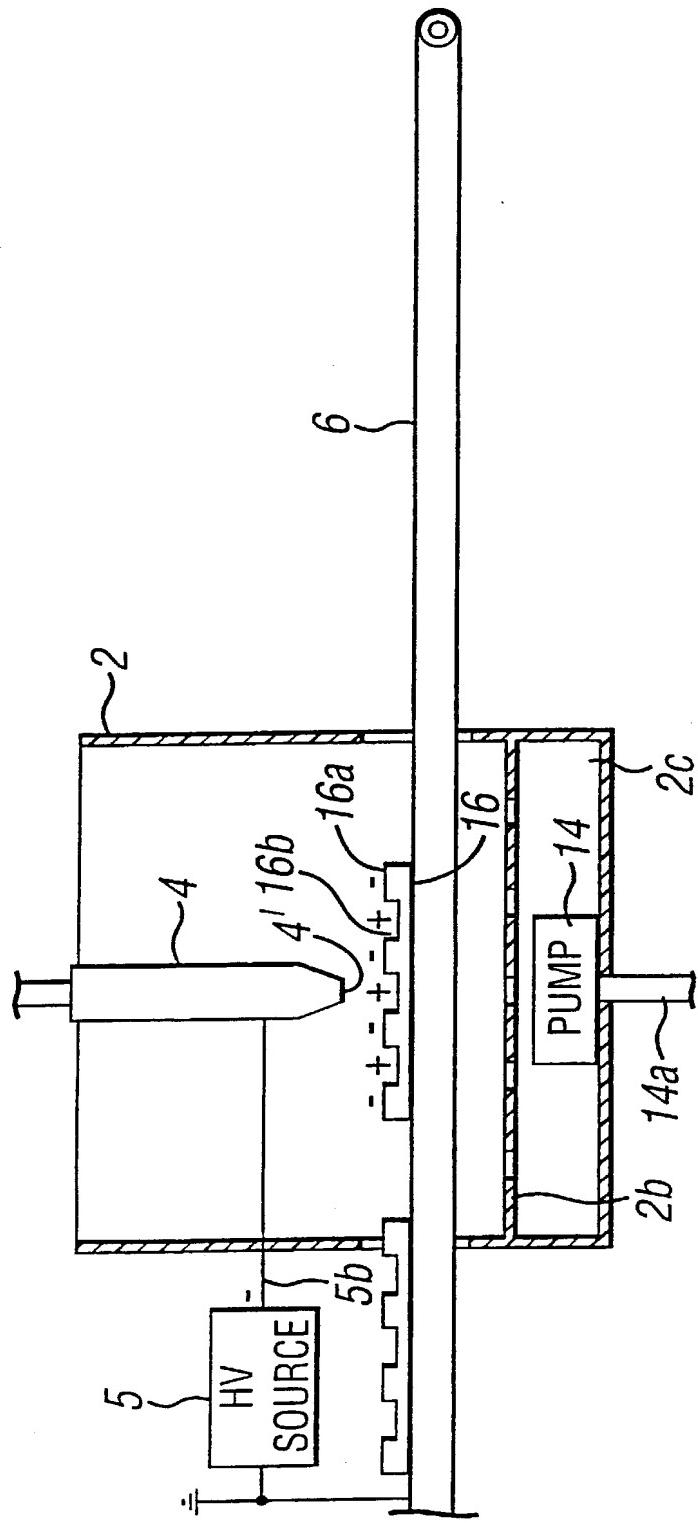
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FIG. 5



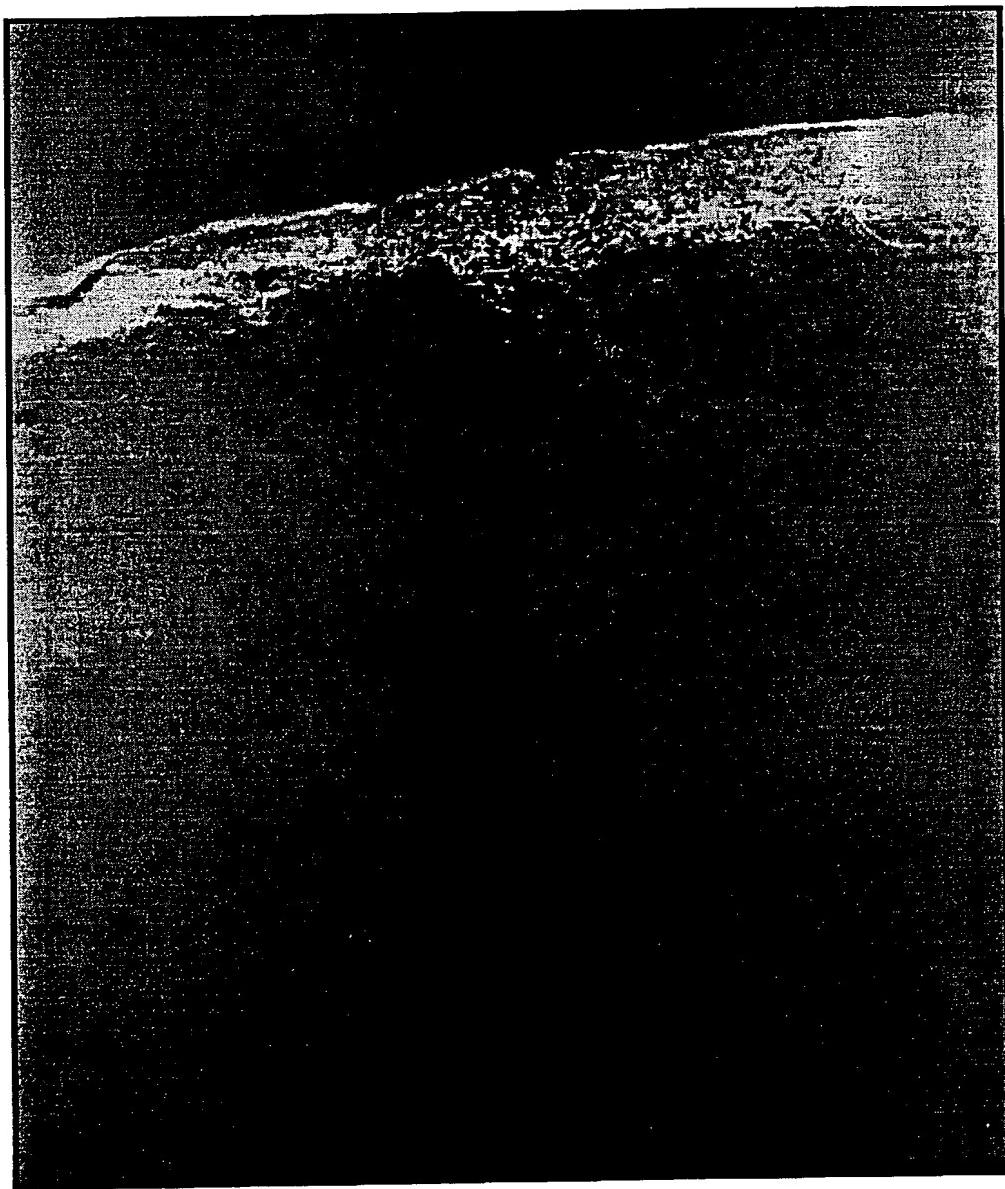
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FIG. 7



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FIG. 8



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FIG. 9



DECLARATION FOR PATENT APPLICATION

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled A METHOD AND APPARATUS FOR MANUFACTURING DISSOLVABLE TABLETS, the specification of which is attached hereto unless the following checked:

was filed on 5 May 2000 as United States Application Number or PCT International Application Number PCT/GB00/01728 and was amended on _____ (if applicable)

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above. I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, § 1.56. I hereby claim foreign priority benefits under Title 35, United States Code, § 119(a)-(d) of any foreign application(s) for patent or having a filing date before that of the application on which priority is claimed.

Prior Foreign Application(s):

| 9910505.8 | 6 MAY 1999 | Priority Claimed |
|-----------|------------------------|---|
| (Number) | (Day/Month/Year Filed) | <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No |
| (Number) | (Day/Month/Year Filed) | <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No |

I hereby claim the benefit under Title 35, United States Code, § 119(e) of any United States provisional application(s) listed below.

| Application Number | (Filing Date) |
|----------------------|---------------|
| (Application Number) | (Filing Date) |

I hereby claim the benefit under Title 35, United States Code, § 120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, § 112, I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, § 1.56 which became available between the filing date of the prior application and the national or PCT International filing date of this application.

| (Application Number) | (Filing Date) | (Status - patented, pending, abandoned) |
|----------------------|---------------|---|
| (Application Number) | (Filing Date) | (Status - patented, pending, abandoned) |

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I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statement and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

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Inventor's signature [Signature] Date: 26.06.01

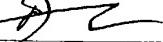
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Additional inventors are being named on separately numbered sheets attached hereto.

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